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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,538	05/03/2001	Brita Schulze	047664-5002-US	4013
9629 7590 01/17/2007 MORGAN LEWIS & BOCKIUS LLP 1111 PENNSYLVANIA AVENUE NW WASHINGTON, DC 20004			EXAMINER SOROUSH, LAYLA	
			ART UNIT	PAPER NUMBER
			1617	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		01/17/2007	PAPER	

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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**Office Action Summary**

Application No.

09/847,538

Applicant(s)

SCHULZ, BRITA

Examiner

Layla Soroush

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on August 28, 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 58-61, 63, 67, 69 and 74 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 58-61, 63, 67, 69, and 74 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

***DETAILED ACTION***

The response filed August 28, 2006 presents remarks and arguments submitted to the office action mailed March 27, 2006 is acknowledged.

Applicant's amendments submitted August 28, 2006 is acknowledged wherein claims 58-59, 63, 67, 69 and 74 are amended. Claims 58-61, 63, 67, 69, and 74 are pending.

Applicant's arguments over the ODP rejection of claims 58-61, 63, 67, 69, and 74 of copending applications 10/519, 193 and 11/018574 is not persuasive. Therefore, the rejection is maintained for reasons of record.

Applicant's arguments over the 35 U.S.C. 112, 2<sup>nd</sup> paragraph rejection of claim 61 is persuasive. Therefore, the rejection is herewith withdrawn.

Applicant's arguments over the 35 U.S.C. 102 (b) rejection of 58-59, 61, 63, 67, 69, and 74 over Unger (US Pat No. 5,770,222) is not persuasive. Therefore, the rejection is maintained for reasons of record.

Applicant's arguments over the 35 U.S.C. 102 (e) rejection of 58-59, 63, 67, and 74 over Thierry (US Pat No. 6,110,490) is not persuasive. Therefore, the rejection is maintained for reasons of record.

Applicant's arguments over the 35 U.S.C. 103 (a) rejection of 60 over Thierry (US Pat No. 6,110,490) or Unger (US Pat No. 5,770,222) is not persuasive. Therefore, the rejection is maintained for reasons of record.

The rejection is restated below for applicant's convenience.

***Double Patenting***

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The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969). A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 58-61, 63, 67, 69, 74 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 51- 59 of copending Application No. 10/519,193 and claims 1-15 of copending Application No. 11/018574. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are directed to overlapping inventions.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. The instant application is directed to methods of modifying a therapeutic agent comprising associating the agent with one or more cationic component to produce a composition having optimal range of zeta potential and dispersing the composition in a medium to form colloids having a size of about 10 nm to about 400 nm, wherein the composition exhibits a specific zeta potential and comprise liposomal moieties. Both sets of copending applications are directed to

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methods of producing a liposomal preparation comprising a therapeutic agent such as a taxane derivative and a cationic lipid, wherein the liposomes particle size ranges between 50nm to 400nm. The instant claims only differ in reciting the desired zeta potential. However such properties can be optimized by routine experimentation to maximize efficacy of the therapeutic agent. Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to practice the scope of the instant claims when in possession of the claims in the copending application.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 58-59, 61,63, 67, 69, 74 are rejected under 35 U.S.C. 102(b) as being anticipated by Unger US Patent 5,770,222.

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The instant claims are directed to methods of modifying a therapeutic agent comprising associating the agent with one or more cationic component to produce a composition having optimal range of zeta potential and dispersing the composition in a medium to form colloids having a size of about 10 nm to about 400 nm, wherein the composition exhibits a zeta potential in the range of about +30 mV to +65 mV in about 0.05 mM KCL solution at about pH 7.5.

Unger teaches methods of preparing cationic liposomal therapeutic system comprising a bioactive agent such as taxol (abstract, col 8, lines 25-55; col 49, line 65). The cationic lipids employed by Unger include DOTAP or DOPC which meets the limitations of the instant claim 74. (see col 8, lines 25-29; col 9, lines 24-26; col 36, line 25-col 37, line 67). Unger's particle size range between 30 nm to 5 microns which falls within the instantly described particle sizes (see col 15, lines 5-20). Further, the systems of Unger form a colloidal suspension when placed in an aqueous medium (see col 15, lines 36-67; col 43, line 64-col 46, line 20; col 48, lines 7-10).

Applicant is informed that a prior art composition that comprise all elemental components of the instantly created composition would meet all functional characteristics of the created composition, because such characteristics are inseparable from the composition. Unger meets all elemental steps of the instant claims and the compositions created thereof. Since Unger's compositions was prepared by the same steps as the instantly claimed process and further comprise all elemental components of the instantly prepared composition, they would inherently exhibit the same zeta potentials and targeting properties as those instantly claimed, because such functional

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characteristics of the created composition is inseparable from the describe composition of Unger.

Any cationic components that exhibit magnetic properties can fall within the scope of such limitation. Unger discloses and even claims the use of metallic salts and complexes with the cationic lipid moieties either as free radicals generator or as blood products. (col 13, lines 24-55; col 50, lines 7-8). Thus, Unger anticipates such limitation.

Claims 58-59, 63, 67, 69, 74 are rejected under 35 U.S.C. 102(e) as being anticipated by Thierry US Patent 6,110,490.

Thierry teaches methods of preparing drug containing liposomes wherein the specific lipids used in the liposomes are cationic. (see abstract; col 9, lines 5-67; col 30, lines 10-22). Thierry specifically teaches cationic lipids such as DOPE which meets the limitations of claim 74. Thierry's method prepares targeted drug delivery liposomes that can target vascular sites (see col 10, line 45-60; col 11, line 30). The therapeutic agents that are modified by Thierry's method include various cytotoxic drugs such as taxol; which is a taxane compound. (see col 8, line 1-9; col 12, line 13). The therapeutic agents used by Thierry are encapsulated in the liposomes and are suspended in an aqueous medium to form liposomes to having a size in range of 200- 3000nm (see col 25, lines 24-46). Such range of particles falls within the scope of the instantly created particles.

Thierry meets all elemental steps of the instant claims and the compositions created thereof. Since the compositions prepared by Thierry meets all elemental

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components of the instantly prepared composition, they would inherently exhibit the same zeta potentials as instantly claimed, because such functional characteristics of the

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1,148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 60 is rejected under 35 U.S.C. 103(a) as being unpatentable over Thierry or Unger.

The teachings of both Thierry and Unger were described above. They only fails to explicitly state that their employed cationic component comprises molecules having an isoelectric point above 7.5 or that the composition as a whole has an isoelectric point above 7.5.

Nevertheless, since cationic lipids by definition must have a isoelectric point above 7 (see instant specification, pg. 15, at para 0057), absent a showing of



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unexpected results, it would have been obvious to one of ordinary skill in the art at the time of invention to optimize such parameters during the processes described by either Thierry or Unger by routine experimentations. The ordinary skill in the art would have been motivated to do such optimization to improve stability and delivery of such systems.

### ***Response to Arguments***

Applicant's arguments filed August 28, 2006 have been fully considered but they are not persuasive for the reasons set forth below.

In response to the argument's made over the ODP rejections of copending applications 10/519,193 and 11/018574, Examiner respectfully reiterates " Both sets of copending applications are directed to methods of producing a liposomal preparation comprising a therapeutic agent such as a taxane derivative and a cationic lipid, wherein the liposomes particle size ranges between 50nm to 400nm. The instant claims only differ in reciting the desired zeta potential. However such properties can be optimized by routine experimentation to maximize efficacy of the therapeutic agent. Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to practice the scope of the instant claims when in possession of the claims in the copending application."

Applicant's arguments over the 35 U.S.C. 112, 2<sup>nd</sup> paragraph rejection of claim 61 is persuasive. Therefore, the rejection is herewith withdrawn.

In regards to the arguments made over Unger and Thierry, the examiner respectfully reiterates: Applicant is informed that a prior art composition that comprise

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all elemental components of the instantly created composition would meet all functional characteristics of the created composition, because such characteristics are inseparable from the composition. The references meet all elemental steps of the instant claims and the compositions created thereof. Since reference's compositions are prepared by the same steps as the instantly claimed process and further comprise all elemental components of the instantly prepared composition, they would inherently exhibit the same zeta potentials and targeting properties as those instantly claimed, because such functional characteristics of the created composition is inseparable from the describe composition of the references.

Applicant's argue that the presently claimed invention is effective for selective targeting to an activated vascular site. Unger teaches "using the method of the invention, therapeutic delivery may be effected in a patient's heart, and a patient's vasculature (that is, venous or arterial systems). The invention is also particularly useful in delivering therapeutics to a patient's left heart, a region not easily reached heretofore with therapeutic delivery." Therefore, the prior art teaches the effect of the drug on the vascular site, and hence meets the limitation of the instant claims. Additionally, the Thierry reference teaches, "The liposomal delivery system of the present invention makes possible high transduction efficiency" in for example human vascular endothelial cells; hence meeting the limitations of the instant claims.

The arguments are not persuasive and the rejection is made **FINAL**.

**THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

***A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.***

#### **Conclusion**

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-5008. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

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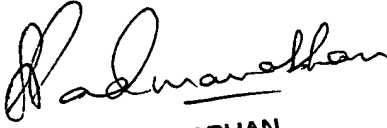
published applications may be obtained from either Private PAIR or Public PAIR.

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you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free).



SREENI PADMANABHAN  
SUPERVISORY PATENT EXAMINER